

(GenBank accession number AAC57106 (gi:1718277), which is incorporated herein by reference) (SEQ ID NO:29) and amino acids 8 through 117 of WNV Cp protein (SEQ ID NO:30); 3) amino acids from an internal portion of Ebola virus nuclear protein (GenBank accession number AAG40164 (gi:11761746), which is incorporated herein by reference) (SEQ ID NO:31) and amino acids 10 through 117 of WNV Cp protein (SEQ ID NO:32); 4) amino acids from an internal portion of Ebola virus glycoprotein (GenBank accession number AAA96744 (gi:1141779), which is incorporated herein by reference) (SEQ ID NO:33) and amino acids 4 through 23 of WNV Cp protein (SEQ ID NO:34); 5) amino acids from another internal portion of Ebola virus glycoprotein (SEQ ID NO:35) and amino acids 50 through 73 of WNV Cp protein (SEQ ID NO:36); and 6) amino acids from an internal portion of Rubella virus capsid protein (GenBank accession number GNWVR4 (gi:74519), which is incorporated herein by reference) (SEQ ID NO:37) and amino acids 64 through 114 of WNV Cp protein (SEQ ID NO:38). The proapoptotic protein comparisons are as follows: 1) amino acids from an internal portion of the human BAK protein (GenBank accession number Q16611 (gi:2493274), which is incorporated herein by reference) (SEQ ID NO:39) and amino acids 17 through 63 of WNV Cp protein (SEQ ID NO:40); 2) amino acids from an internal portion of the human Bcl-2 associated X protein (GenBank accession number XP_009093 (gi:15304386), which is incorporated herein by reference) (SEQ ID NO:41) and amino acids 109 through 123 of WNV Cp protein (SEQ ID NO:42); 3) amino acids from an internal portion of the human BIK protein (GenBank accession number XP_015353 (gi:13655199), which is incorporated herein by reference) (SEQ ID NO:43) and amino acids 75 through 118 of WNV Cp protein (SEQ ID NO:44); 4) amino acids from an internal portion of the human BID protein (GenBank accession number XP_009825 (gi:13647251), which is incorporated herein by reference) (SEQ ID NO:45) and amino acids 84 through 95 of WNV Cp protein (SEQ ID NO:46); and 5) amino acids from an internal portion of the human Bad protein (GenBank accession number CAC22429 (gi:12309966), which is incorporated herein by reference) (SEQ ID NO:47) and amino acids 15 through 23 of WNV Cp protein (SEQ ID NO:48). The values in brackets are identity/homology scores, where a maximum possible score is 590. Comparisons and alignments were generated by MacVector.

Figure 19 shows the alignment of the HIV-1 89.6 Vpr protein sequence with portions of the sequences of proteins from other viruses and with portions of the sequences of proapoptotic proteins. The complete sequence of the HIV-1 89.6 Vpr protein (amino acids 1 - 96) appears at

the top in bold. Shown are 7 comparisons of HIV-1 89.6 Vpr protein with other viral proteins and 6 comparisons of HIV-1 89.6 Vpr protein with proapoptotic proteins. The viral protein comparisons are as follows: 1) amino acids from an internal portion of the p230 nonstructural protein of Sindbis virus (GenBank accession number NP_062889 (gi:9790318), which is incorporated herein by reference) (SEQ ID NO:49) and amino acids 22 through 59 of HIV-1 89.6 Vpr protein (SEQ ID NO:50); 2) amino acids 68 through 110 of WNV Cp protein (see description for Fig. 18 above) and amino acids 54 through 95 of HIV-1 89.6 Vpr protein (SEQ ID NO:51); 3) amino acids from an internal portion of the 2A protein of Cucumber mosaic virus (GenBank accession number CAB75953 (gi:7105855), which is incorporated herein by reference) (SEQ ID NO:52) and amino acids 77 through 89 of HIV-1 89.6 Vpr protein (SEQ ID NO:53); 4) amino acids from another internal portion of the 2A protein of Cucumber mosaic virus (SEQ ID NO:54) and amino acids 49 through 67 of HIV-1 89.6 Vpr protein (SEQ ID NO:55); 5) amino acids from an internal portion of the Rubella virus capsid protein (SEQ ID NO:56) and amino acids 38 through 47 of HIV-1 89.6 Vpr protein (SEQ ID NO:57); 6) amino acids from an internal portion of the Nipah virus fusion protein (GenBank accession number NP_112026 (gi:13559813), which is incorporated herein by reference) (SEQ ID NO:58) and amino acids 60 through 72 of HIV-1 89.6 Vpr protein (SEQ ID NO:59); and 7) amino acids from an internal portion of the reovirus core-minor form Mu2 protein (GenBank accession number AAK54467 (gi:14149150), which is incorporated herein by reference) (SEQ ID NO:60) and amino acids 60 through 72 of HIV-1 89.6 Vpr protein (SEQ ID NO:61). The proapoptotic protein comparisons are as follows: 1) amino acids from an internal portion of the mouse BIM protein (GenBank accession number NP_033884 (gi:6753192), which is incorporated herein by reference) (SEQ ID NO:62) and amino acids 7 through 74 of HIV-1 89.6 Vpr protein (SEQ ID NO:63); 2) amino acids from an internal portion of the rat BOD protein (GenBank accession number AAC23593 (gi:3228566), which is incorporated herein by reference) (SEQ ID NO:64) and amino acids 23 through 74 of HIV-1 89.6 Vpr protein (SEQ ID NO:65); 3) amino acids from an internal portion of the mouse Mtd protein (GenBank accession number AAC53582 (gi:2689660), which is incorporated herein by reference) (SEQ ID NO:66) and amino acids 16 through 67 of HIV-1 89.6 Vpr protein (SEQ ID NO:67); 4) amino acids from an internal portion of the human Bcl-2 associated X protein (SEQ ID NO:68) and amino acids 18 through 75 of HIV-1 89.6 Vpr protein (SEQ ID NO:69); 5) amino acids from another internal portion of the human Bcl-2 associated X protein (SEQ ID NO:70) and amino acids 18 through 42 of HIV-1

89.6 Vpr protein (SEQ ID NO:71); and 6) amino acids from an internal portion of the human Bad protein (SEQ ID NO:72) and amino acids 33 through 44 of HIV-1 89.6 Vpr protein (SEQ ID NO:73). The values in brackets are identity/homology scores, where a maximum possible score is 590. Comparisons and alignments were generated by MacVector.

5 DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention arises out of the discovery of the apoptosis-inducing activity of the WNV capsid (Cp) protein in tumor-derived cells. It has been discovered that expression of WNV capsid protein in cells in culture leads to the induction of an apoptotic pathway and, ultimately, to the death of hyperproliferating cells. It has also been observed that a 22 amino acid residue peptide from the carboxy-terminal region of WNV Cp protein has apoptosis-inducing activity. The apoptosis-inducing activity of WNV capsid protein renders Cp protein, and functional fragments thereof, useful in methods of killing rapidly growing cells, including cancer cells, and in screening systems to identify compounds that inhibit the apoptosis-inducing activity, which may be used for treatment of WNV infection.

The virus family *Flaviviridae* is composed of positive-sense, single-stranded RNA genome viruses classified into three genera: *Pestiviruses*, which include bovine diarrhea virus (BVDV), "Hepatitis C-like viruses," which include hepatitis C virus (HCV), and *Flaviviruses*. The *Flavivirus* genus includes at least ten serologically-defined subgenus groups, as well as unclassified viruses. WNV is a member of the mosquito-borne Japanese encephalitis virus group, which also includes, among others, Japanese encephalitis virus (JEV) and St. Louis encephalitis virus (SLEV), that are highly related to WNV. Other *Flaviviruses* include Yellow fever virus (YFV) and Dengue viruses (DENV), which are in different subgenus groups. Nucleotide and amino acid sequence analyses reveal conservation of sequences within and between serogroups. The WNV Cp protein shares homology with capsid and other proteins of other viruses, including, but not limited to, viruses in the *Flaviviridae* family, and viruses from many other virus families. The WNV Cp protein also shares homology and with other proteins, including, non-viral proteins, including proapoptotic proteins of mammalian origin.

In some embodiments of the invention, the capsid protein is derived from a *Pestivirus*. In some embodiments of the invention, the *Pestivirus* from which the capsid protein is derived is BVDV. In some embodiments of the invention, the capsid protein is derived is from a *Flavivirus*. In some embodiments of the invention, the *Flavivirus* from which the capsid protein